

A. HDAC4

MSQSHPHQSGRDGPVELLPANPVRNMPSTVDVATALLPQVAPSVHMDLRHOFSLPVAEPALREQOQOELLALKQKQOIRILL 90
AefforQEHLSRQQLQHEHQQOQMLHQQLLEHQRKLEHRQOELEKHQKQOELLKQKQESASVSTEVRKQGEPL 180
NKKOOLANLHNHICISDTPVWGTCQHSLSQSPSGQSVSTNHPVLCQAKDDPFLKATASQVQVQVQVQVQVQVQVQV 270
RKGDPVYTLALRQISVDSQSSASQSPSGPSSNSQSVSAENIADVPSTIPATSLAHRLVAVRQESAAPIPLTSSPTINLTGLPA 360
TCSAGTACQCEHMLTIPALQOQLSFGTGLTIPLSTELPDEGGCAASPLIQRVLEQFQVATLGTGQALPHQASLVGADRS 450
PSHLKRLRQFLKRTQASLPONALQOHLVHQOQHQRLEKHKQOQOQOQOQOQOQOQOQOQOQOQOQOQOQOQOQOQOQO 540
LDRLPQKQKQAAHQVQKQEPLESEDEEAEPPEVEFGQROQSPQELLFRMQLLLEQQRHOLNQAQSHMAMGVPFSGQPLPSRA 630
QSSPASAFTPVSGQVPTKPRFTTGLVLTLMHQQLTCCSSSSSHPEHNRQISMSRRLQGTGLRQKCECIRGSRATLELQVHSER 720
LVGTNPRLKQKQDLKGLSLASVPLPCGQGVDSSTIINETHSAGARLANVQGVLEFVATLQKQSLRQVAPRSHAEESTPM 810
GCFYTSVAVAAQLQKLSLVLVDVDEHGTQOAFSTPMLRLRYDQVETFGSCGAPVEQVGTGCVGFVNMMAFTGCLD 900
PQKQVLEAFTPTWQVPLSEPARQVVLVSSGFAVEGHTPPLGYNLSARCFVLTQKQLAGCRVILAEGLGDDITADCSAECS 990
ALLGHELDLEPKVLQOQNPANVARSKMEIHSYKRCILQRTISTACRSILEAQTCENEAETVTANASLVQVPAKPRDEEPMEE 1080
EPLP. 1085

B. HDAC5

MNSPNSDQCKSREPLSLILPTSLHSIPVTVEKVPVLPAMPSSHQGGGSSPVELRGLQGVSDPTLRQOQLQOELLALKQOQOGL 90
KQLLFAEFQKHLHTRQGVLEQLOKQLKQOQMLAAKQOQLLEAAQOQLLEQQRQOQOQOQOQOQOQOQOQOQOQOQOQO 180
TEVYLRLQOFLSISKEKPTGGHLSLPHFYKQAGHARSQSPSGQSPCTPRQYRQLPGYDSRDQFLPKRTASVHSVRSRLK 270
QOAKERRSSPLLRQGTQVISTFORAVEITQCGGASSVNSAPGSSPSSMSTIAENGFTQSVNHPITLQKQALRQGLRQGL 360
FSLYTSPLNHSILSGQATVVTNHSILXSLKSTQOEAERQALQSGTGKSTTKXPSSTSIKCLLOLQAGCGSSGQVQVQV 450
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LFRQPTTHPEESTELTEQGVLELQALNMPRESTESTQGTLEEDKEEDKEEDKEEDMTQVQDEGESGASQVLEDPGAGVQ 720
SDQQLPQVQVQVLSLTVPRQALQSGSPALQAGHRSPPQOQVLTGVVTHYTHQKQGTTHVPEHAGRIQSTNSRQLK 810
TGLLSKEKIRKQKATLDETVHSEHTLTXGTSPLNRKQSLDQKGLGTQKQVLAHQLQGVQVSDTVNTHSSSVAHVACGLLS 900
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MLTAGCRVILAEGLGDDITADCSAECSALLSLOVLEQVLEFVATLQKQSLRQVPAKPRDEEPMEE 1080
EENETVSANLLSVGACQAGQAAHARSIPRAEPMEQPL. 1123

C. HDAC6

MTSCQGSTTTRRRSRNQSPQPSDSSVTSKRNIKKQAVPSTPHLAEVKKQKMKKQLQAAEEDLTVLQGLMDLNLAEALAGTLVL 90
DEQLNEHGLMDDSPGEPERHILAEQLOQELLDRCVSFAARFAEELVMSHLEVDIQRHETQVHNEGLRVADTQVSTVLPHS 180
YSCALASSGVSLVDVLAEGIRNMAIIRPPGBAAQSLSDQGVCMFHHVAALQAGHRIKVLTVDDVHVPQGVQGTTPQDP 270
LYFSIRYERGQVPLHKAASMTSTQRCQGGQTTINVPVMPQVDEBDVIAFLHVLVLALEFQVLTVAAGFADQKQGVMDA 360
AGFALTLTLMMLQAGLLELQGLNLAAGVSAVSHBQVDEBDVIAFLHVLVLALEFQVLTVAAGFADQKQGVMDA 450
EEDVWSEEGQCPHMLPTLWVQSLTGLVVDQNDQHQLSDHSHVLPQRLIRNCRLELGLAGRLCLTLTPRPAATELICH 540
SAEYVGLDTEKMTKREHRESSNFTSIVCTPFCFACVLAQCAACRLVAGSEVLNAAVVRPGBHEDQDACCFDFNSVAAA 630
RHAGTQSHGLRLILVDMVDEQGTQMFDEDFVSLYSLRQYGTFFPMQDEGASSQAGAGTQGVVNAVNGAGTQADTLAAH 720
RLVLPIATEFNPVLVLSVAGFADQGLQGCQSPGEGVHLTLHGLASRLITLILEGNNYLSIESHMAKQVILVDRPRLN 810
PPLSGALASTITEVHRRYVRSRLVMKDEBERSSSKLTKVQAQAPRIALRNTREKVLVDEHETQVAGLADQGTSEAGVAGT 900
AVVALTGQDSEATGAGTATQATISAAIGAGMLQSSSTNITQYTLASTSTNGTQVSTPVGCTTQIPSTLISQILTELGSESSQAGSAGNELNGA 1080
AGQGWADSHSGTCGLLQATIFAYVPLPCPHLVAVCPILPAAGLDVQPCQGDQIGENWCLCSQVYQVIRINGLHQHNSGH 1170
PLVLSYIDLSAWVCYQVAVHQIALLDVNTQNLQNKNGDEMPHPI. 1216

100 HAAKSEAGSGCFVNDVILAILELKKV... -ORVILVDTIHMDGQVEAPPTTIDRVMTVSRHXY--GEYFFGT 208
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104 HAAEESTPMFGCFVNSVAVAKLLQORLSV-K-ILTVLDVYVHNGNGTQOAFYSVYLTMLERHNDYDHDFFFG 305
200 HAAEESTAMGCFVNSVAVITAKLQOQLNVG-K-VLVLVDVYHNGNGTQOAFYHNDYDHDFFFG 368
210 HAAHOSLMDGCFVNSVAVAAVYQXKHRR-R-VLVMVYVHNGNGTQOAFYHNDYDHDFFFG 410
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228 HAAEESTAMGCFVNSVAVAAVYQXKHRR-R-VLVMVYVHNGNGTQOAFYHNDYDHDFFFG 529
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232 HAAEESTAMGCFVNSVAVAAVYQXKHRR-R-VLVMVYVHNGNGTQOAFYHNDYDHDFFFG 555
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282 HAAE

Figure 2

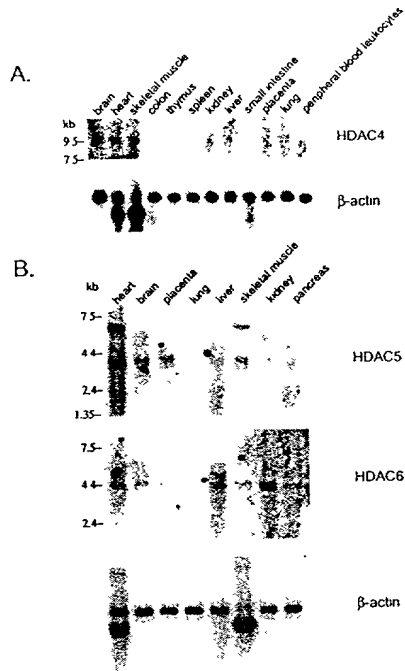
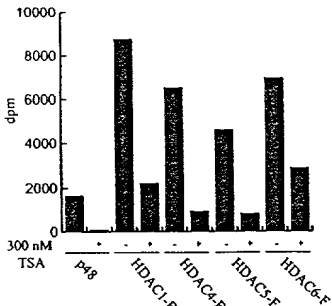


Figure 3

A.



B.

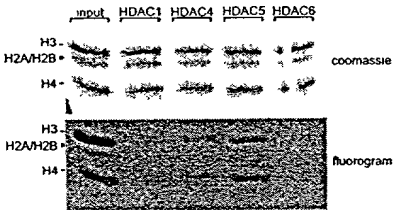


Figure 4

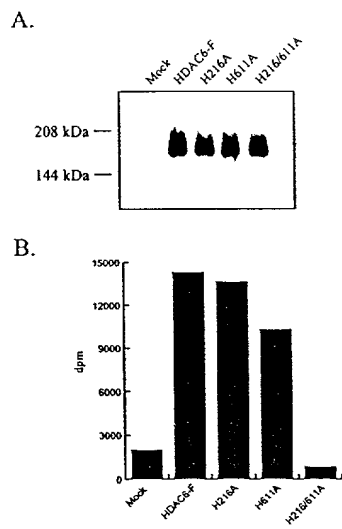


Figure 5

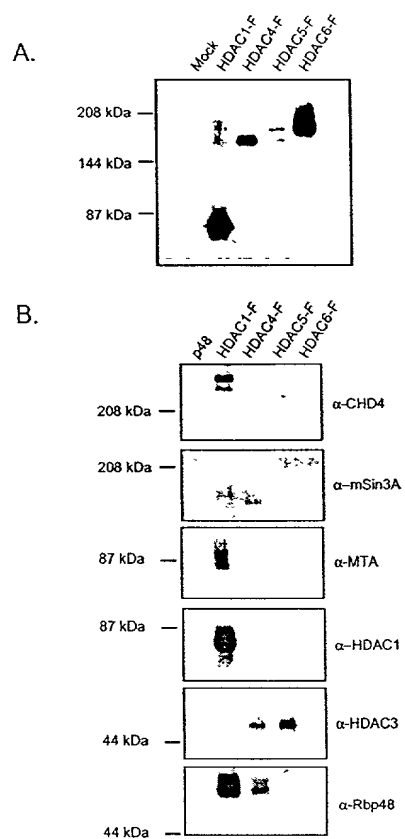


Figure 6

A.

HOMOLOGY REGIONS	INITIAL AA IN HDAC1	CONSENSUS SEQUENCES	EXCEPTIONS
1	99	D(C/T)P(V/I)F N/A	CLASS I CLASS II
2	134	NXXGGXHH A RPPG H H A	CLASS I CLASS II Hos3p ends in C, AcuC ends in G
3	148	SG(F/Y)CXXN G(F/Y)CXXN	CLASS I CLASS II Hda1 ends in S
4	174	D* D* H H G D G Y (Q/E) D* D* H H G X G T Q	CLASS I CLASS II
5	193	VX T X S H VX (Y/F) S X H	CLASS I CLASS II
6	225	N* P (M/L) X D G I D D X (S/T) Y N/A	CLASS I CLASS II Hos1p has instead: N* P L K H G C D D Y
7	298	* G G G G Y * E G G (Y/H)	CLASS I CLASS II

B.

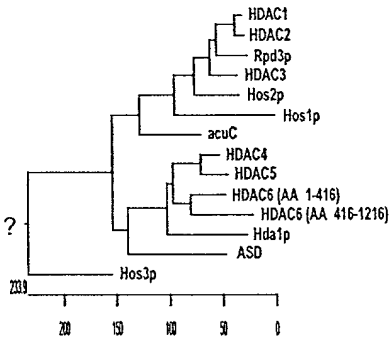


Figure 7

Figure 7A

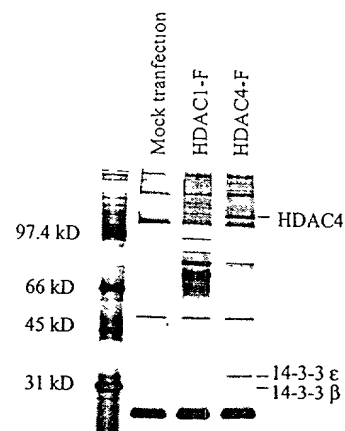


Figure 7B

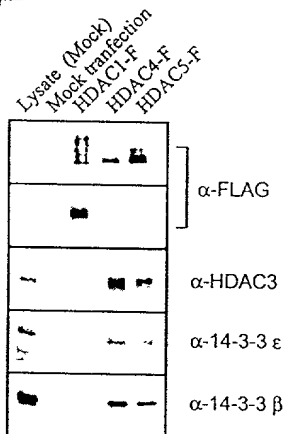


Figure 8

Figure 8A

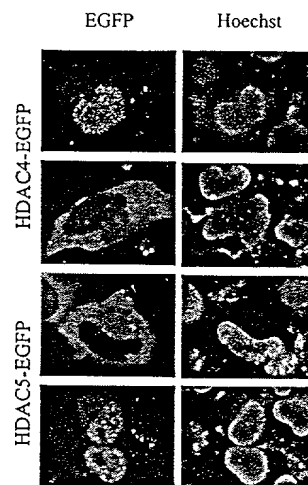


Figure 8B

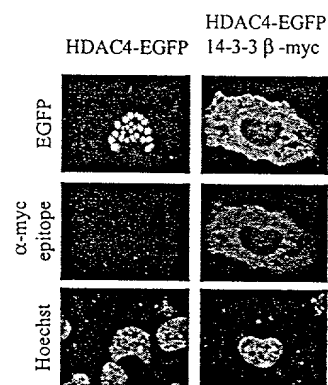


Figure 9

Figure 9A

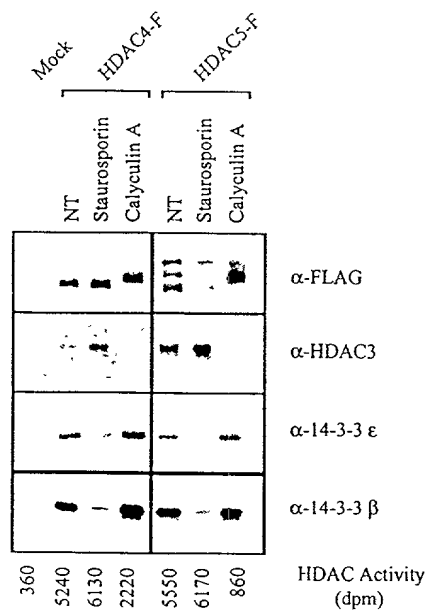


Figure 9B

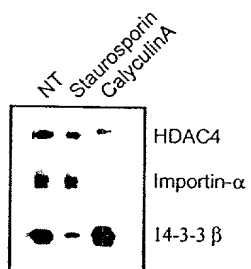


Figure 10

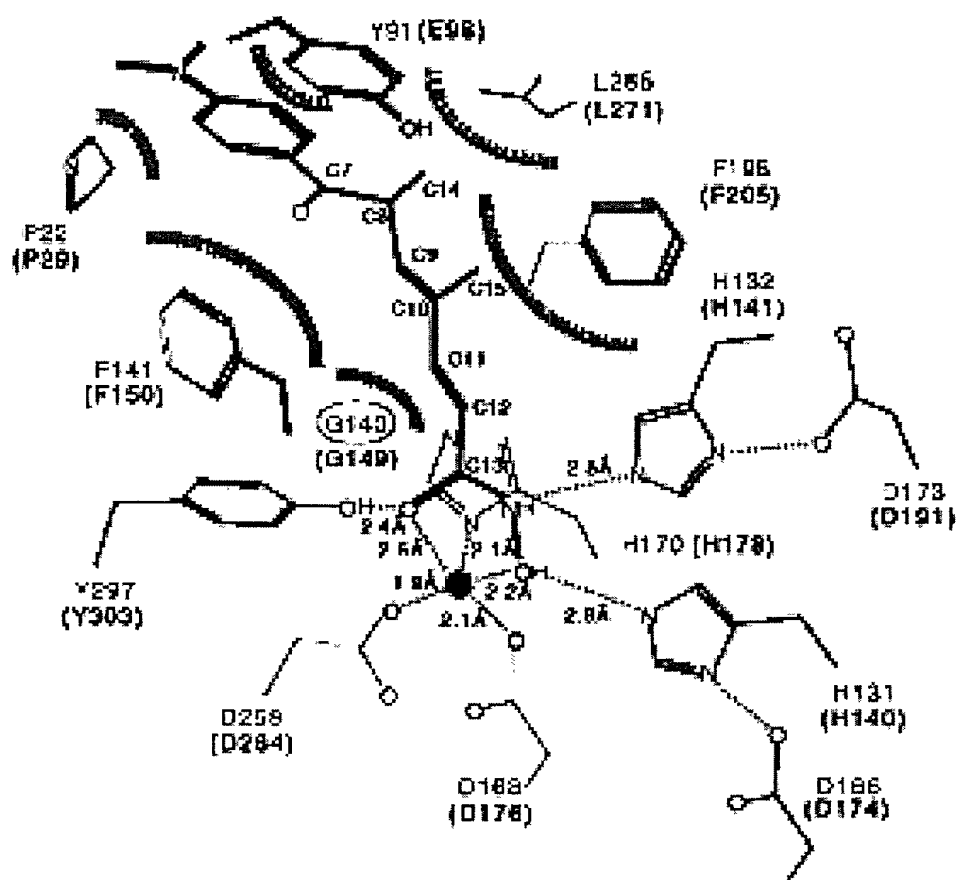


Figure 11

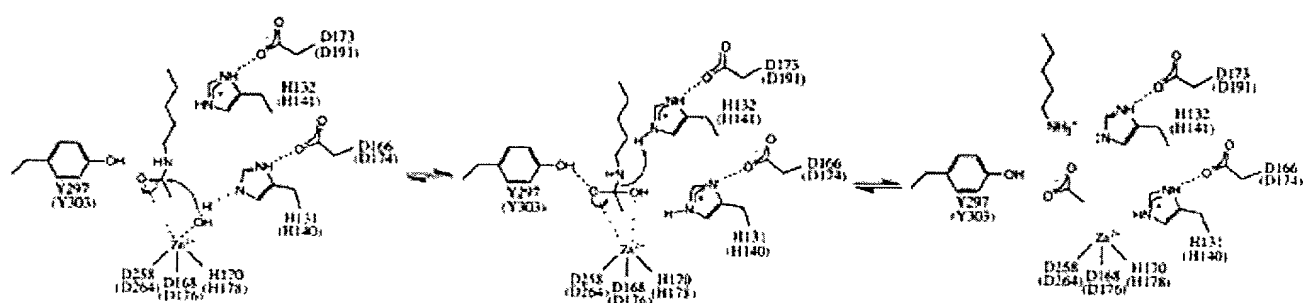
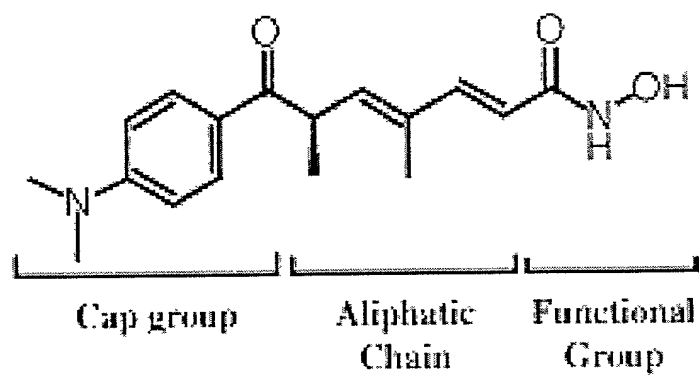


Figure 12



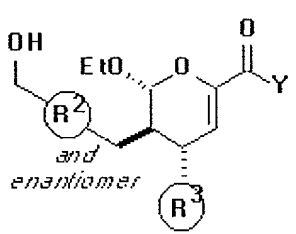
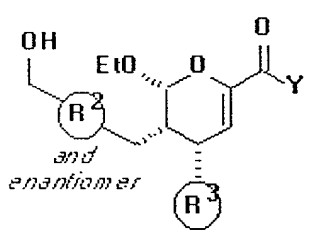
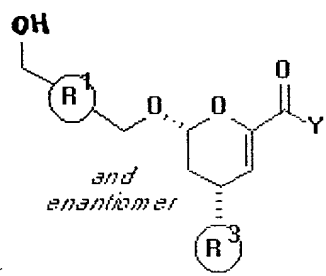
Variable	Mean	SD	Min	Max
Age	38.5	12.5	18	65
Gender	0.5	0.5	0	1
Marital status	0.7	0.5	0	1
Education	12.5	2.5	9	16
Income	15.5	10.5	5	35
Health status	0.8	0.4	0	1
Employment status	0.6	0.5	0	1
Living with family	0.9	0.3	0	1
Number of children	1.5	1.5	0	5
Number of siblings	2.5	2.5	0	10
Number of parents	2.0	2.0	0	4
Number of grandparents	2.0	2.0	0	4
Number of great-grandparents	2.0	2.0	0	4
Number of other relatives	2.0	2.0	0	4
Number of friends	2.0	2.0	0	4
Number of acquaintances	2.0	2.0	0	4
Number of neighbors	2.0	2.0	0	4
Number of colleagues	2.0	2.0	0	4
Number of business contacts	2.0	2.0	0	4
Number of professional contacts	2.0	2.0	0	4
Number of social contacts	2.0	2.0	0	4
Number of community contacts	2.0	2.0	0	4
Number of religious contacts	2.0	2.0	0	4
Number of political contacts	2.0	2.0	0	4
Number of cultural contacts	2.0	2.0	0	4
Number of sports contacts	2.0	2.0	0	4
Number of hobby contacts	2.0	2.0	0	4
Number of volunteer contacts	2.0	2.0	0	4
Number of mentor contacts	2.0	2.0	0	4
Number of role model contacts	2.0	2.0	0	4
Number of inspirational contacts	2.0	2.0	0	4
Number of motivational contacts	2.0	2.0	0	4
Number of supportive contacts	2.0	2.0	0	4
Number of encouraging contacts	2.0	2.0	0	4
Number of uplifting contacts	2.0	2.0	0	4
Number of inspiring contacts	2.0	2.0	0	4
Number of motivating contacts	2.0	2.0	0	4
Number of empowering contacts	2.0	2.0	0	4
Number of enabling contacts	2.0	2.0	0	4
Number of facilitating contacts	2.0	2.0	0	4
Number of assisting contacts	2.0	2.0	0	4
Number of helping contacts	2.0	2.0	0	4
Number of supporting contacts	2.0	2.0	0	4
Number of promoting contacts	2.0	2.0	0	4
Number of advancing contacts	2.0	2.0	0	4
Number of uplifting contacts	2.0	2.0	0	4
Number of inspiring contacts	2.0	2.0	0	4
Number of motivating contacts	2.0	2.0	0	4
Number of empowering contacts	2.0	2.0	0	4
Number of enabling contacts	2.0	2.0	0	4
Number of facilitating contacts	2.0	2.0	0	4
Number of assisting contacts	2.0	2.0	0	4
Number of helping contacts	2.0	2.0	0	4
Number of supporting contacts	2.0	2.0	0	4
Number of promoting contacts	2.0	2.0	0	4
Number of advancing contacts	2.0	2.0	0	4
Number of uplifting contacts	2.0	2.0	0	4
Number of inspiring contacts	2.0	2.0	0	4
Number of motivating contacts	2.0	2.0	0	4
Number of empowering contacts	2.0	2.0	0	4
Number of enabling contacts	2.0	2.0	0	4
Number of facilitating contacts	2.0	2.0	0	4
Number of assisting contacts	2.0	2.0	0	4
Number of helping contacts	2.0	2.0	0	4
Number of supporting contacts	2.0	2.0	0	4
Number of promoting contacts	2.0	2.0	0	4
Number of advancing contacts	2.0	2.0	0	4
Number of uplifting contacts	2.0	2.0	0	4
Number of inspiring contacts	2.0	2.0	0	4
Number of motivating contacts	2.0	2.0	0	4
Number of empowering contacts	2.0	2.0	0	4
Number of enabling contacts	2.0	2.0	0	4
Number of facilitating contacts	2.0	2.0	0	4
Number of assisting contacts	2.0	2.0	0	4
Number of helping contacts	2.0	2.0	0	4
Number of supporting contacts	2.0	2.0	0	4
Number of promoting contacts	2.0	2.0	0	4
Number of advancing contacts	2.0	2.0	0	4
Number of uplifting contacts	2.0	2.0	0	4
Number of inspiring contacts	2.0	2.0	0	4
Number of motivating contacts	2.0	2.0	0	4
Number of empowering contacts	2.0	2.0	0	4
Number of enabling contacts	2.0	2.0		

Residues on rim of channel										Residues in channel									
		E22 *		Y91		* Y94 *				G140		I141		I198		I265			
Class I	HD1P	P	I	G	G	Y	E	N	P	HD1P	N	G	F	E	-	Y	A	F	P
	HDAC1	P	N	G	-	E	D	C	P	HDAC1	S	G	F	E	-	Y	F	-	P
	HDAC2	P	N	G	-	E	D	C	P	HDAC2	S	G	F	E	-	Y	F	-	P
	HDAC3	P	N	G	-	D	D	C	P	HDAC3	S	G	F	E	-	Y	F	F	P
	HDAC8	A	K	G	-	Y	D	C	P	HDAC8	S	G	F	D	-	G	F	F	P
Class II	HDAC3	P	E	G	V	D	S	D	T	HDAC4	M	G	F	D	G	N	F	F	P
	HDAC5	P	E	G	V	D	S	D	T	HDAC5	M	G	F	D	G	N	F	F	P
	HDAC6(a)	P	E	-	-	-	D	S		HDAC6(a)	D	G	Y	Q	G	R	F	F	P
	HDAC6(b)	P	E	-	-	-	D	S		HDAC6(b)	C	G	F	H	G	T	F	F	P
	HDAC7	P	E	G	V	D	T	D	T	HDAC7	M	G	F	D	G	N	F	F	P

Residues in active site																			
		H131		H132		D166		D168		H170		H258		N297					
Class I	HD1P	P	A	G	G	N	H	H	A	Y	I	D	I	D	A	N	H	C	D
	HDAC1	W	A	G	G	L	H	H	A	Y	I	D	I	D	I	H	H	G	D
	HDAC2	W	A	G	G	L	H	H	A	Y	I	D	I	D	I	H	H	G	D
	HDAC3	W	A	G	G	L	H	H	A	Y	I	D	I	D	I	H	H	G	D
	HDAC8	W	S	G	G	V	H	H	A	Y	Y	D	D	I	D	L	H	H	G
Class II	HDAC3	R	P	P	G	-	H	H	A	I	Y	D	V	D	I	H	H	G	N
	HDAC5	R	P	P	G	-	H	H	A	I	Y	D	V	D	I	H	H	G	N
	HDAC6(a)	R	P	P	G	-	H	H	A	I	Y	D	V	D	I	Y	H	H	G
	HDAC6(b)	R	P	P	G	-	H	H	A	I	Y	D	V	D	I	Y	H	H	G
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Figure 14

14A

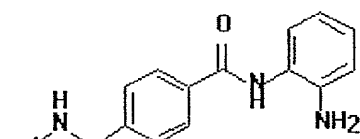
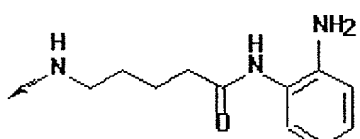
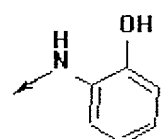
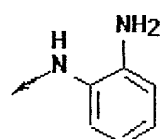


where Y =

#1

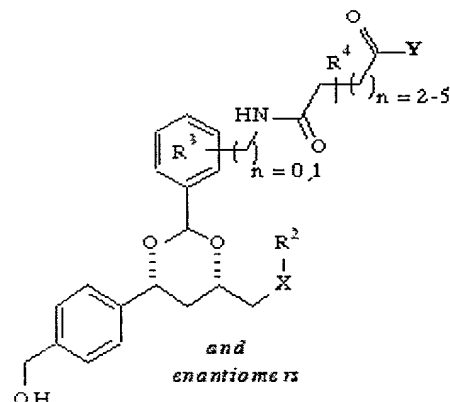
#2

#3



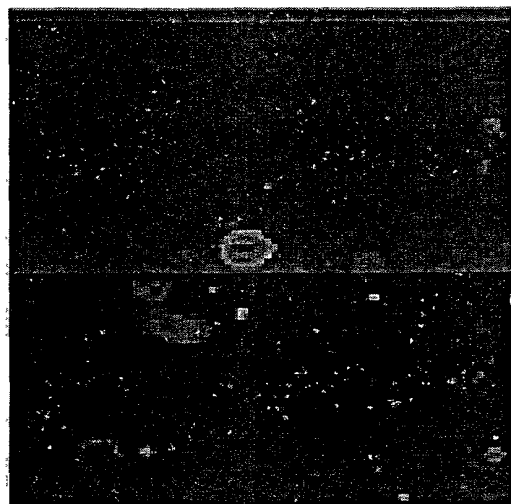
(4 R¹ groups + 2R² groups) \leftrightarrow 10 R³ groups \leftrightarrow 2 (enantiomers) \leftrightarrow 4 amines = 640 compounds

14B



where Y = OH, NHOH, o-aminoaniline

Figure 15



TOSSOE" 28T00860

Figure 16

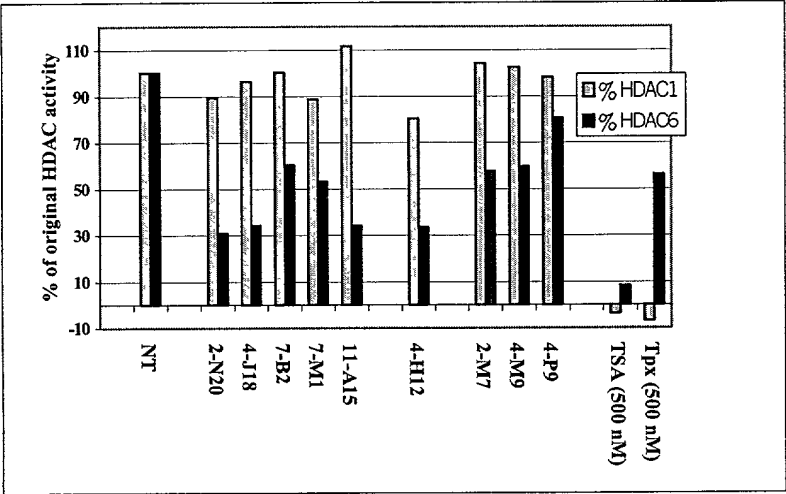


Figure 17

